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AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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57 ASPIRINS

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23357 ASPIRIN
                  (ASPIRIN OR ASPIRINS)
T.1
         31422 "ACETYLSALICYLIC ACID" OR ASPIRIN
=> s L1 and (topical or ointment or external)
         51448 TOPICAL
             41 TOPICALS
         51467 TOPICAL
                  (TOPICAL OR TOPICALS)
         12795 OINTMENT
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         22066 OINTMENT
                 (OINTMENT OR OINTMENTS)
        287281 EXTERNAL
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L2
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=> s L2 and pain
         61237 PAIN
          1553 PAINS
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L3
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            10 L5 AND (0.05% OR 80%)
=> d 16 1-10 ibib ab
     ANSWER 1 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                          2005:679034 CAPLUS
TITLE:
                          Extracts of flowers of carthamus tinctorius and
                          analgesis agents containing them
                          Huh, Moon Young; Kim, Hyun Pyo
Samchully Pharm. Co., Ltd., S. Korea
INVENTOR(S):
PATENT ASSIGNEE(S):
SOURCE:
                          Repub. Korea, No pp. given
                          CODEN: KRXXFC
DOCUMENT TYPE:
                          Patent
LANGUAGE:
                          Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 202319	В1	19990615	KR 1998-59882	19981229 <

KR 193906 B1 19990615 KR 1996-39952 19960914 <--PRIORITY APPLN. INFO.: KR 1996-39952 A 19960914

AB PURPOSE: An extract containing Kaempferol-3-0-rutinoside as an active component extracted from flower of Carthamus tinctorius and an anodyne containing the same are provided, which have a pain-killing effect about two times more than that of aspirin. CONSTITUTION: A flower of Carthamus tinctorius extract contains 0.1 to 0.5% by weight of Kaempferol-3-0-rutinoside, 0.01 to 0.1% by weight of astragalin, and 0.05 to 0.3% of rutin and a pharmaceutically acceptable carrier. The extracts have been formulated into a tablet, a capsule, a soft capsule, a liquid, an ointment or an injection.

L6 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:466643 CAPLUS

DOCUMENT NUMBER: 139:26666

TITLE: Composition for topical application to skin

INVENTOR(S): McClung, Jackie H.

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 14 pp., Cont. of U. S. Ser. No. 82,566,

abandoned CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

US 6579543 B1 20030617 US 2002-153057 20020521 <-
PRIORITY APPLN. INFO.: US 2002-82566 B1 20020222

AB Disclosed is a composition for topical application to an animal's skin for relief from a variety of symptoms caused by medical conditions or phys. injuries. The composition includes at least one compound having analyseic

activity, at least one compound having anti-inflammatory activity, at least one compound having antioxidant activity, at least one compound having anti-neuralgic activity, at least one compound having blood circulation promotion activity, and at least one compound having antidepressant activity. A method for relieving pain by topical application of the composition is also provided. For example, a topical composition contained whole leaf aloe vera concentrate 60, purified water 23.05, MSM 5.0, Emu oil 5.0, Arnica extract 4.0, SD-Alc.-40 1.0, sorbitol 0.70, menthol 0.10, glucosamine HCl 0.1, sodium chondroitin sulfate 0.1, Capsicum Oleoresin 0.1, nettle extract 0.1, Coriander oil 0.1, Kava Kava extract 0.1, exts. of Blue Bottle, Roman chamomile, marigold and lime tree 0.1, willow bark extract 0.1, witch hazel extract 0.1, Carbomer-940 0.1, triethanolamine 0.1, and ascorbyl palmitate 0.05

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:516594 CAPLUS

DOCUMENT NUMBER: 137:83650

TITLE: Salicylic acid derivatives as topical

analgesics

INVENTOR(S): Van Engelen, H. Wayne; Van Engelen, Patricia A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 5 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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KIND DATE APPLICATION NO. DATE
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                                                               _____
    US 6416772
                       B1 20020709 US 2001-759970
                                                               20010112 <--
    US 20020094343 A1 20020718 WO 2002072037 A1 20020919
                                         WO 2002-US731
                                                               20020110 <--
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            CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
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            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
            RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
            YU, ZA, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
            CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
    AU 2002235345 A1 20020924 AU 2002-235345 20020110 <--
RITY APPLN. INFO::

WO 2002-US731 W 20020110
PRIORITY APPLN. INFO.:
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AB A liquid composition permeating skin to relieve pain comprises alc. 57-91%, glycerin 1-12%, an analgesic agent, i.e., a salicylic acid derivative 2-28%, methylsulfonylmethane 0.02-5%, and emu oil 0.01-3%. The composition further comprises, as an addnl. feature, aloe vera 0.05 -4%. The composition features transdermal pain relief such that a patient can apply the analgesic agent directly to an area of pain without such side effects as stomach irritation which is normally associated with aspirin. The composition may be sprayed or rolled directly onto the painful area. Because of the unique formula, the composition is safe to vital internal organs, requires no mixing before use, and is shelf stable for marketing purposes. For example, a test solution was applied to the skin of a woman with a headache. Minutes later the pain from the headache had subsided. She was able to then continue on with her daily routine free of headache pain.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:409811 CAPLUS

DOCUMENT NUMBER: 137:15485

TITLE: Topically applied aspirin decreases

histamine-induced wheal and flare reactions in normal and SLS-inflamed skin, but does not decrease itch. A randomized, double-blind and placebo-controlled human

study

AUTHOR(S): Thomsen, J. S.; Benfeldt, E.; Jensen, S. B.; Serup,

J.; Menne, T.

CORPORATE SOURCE: Department of Dermatology, Gentofte Hospital,

University of Copenhagen, Hellerup, DK-2900, Den.

SOURCE: Acta Dermato-Venereologica (2002), 82(1),

30-35

CODEN: ADVEA4; ISSN: 0001-5555

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal LANGUAGE: English

AB Topically applied aspirin has recently been reported to decrease histamine-induced itch in human volunteers. Our aim is to confirm this and to study the antipruritic ability of topical aspirin in inflamed skin. In 24 non-atopic volunteers, an inflammatory skin reaction was induced in forearm skin at 5 different sites by sodium lauryl

sulfate contained in Finn Chambers. Aspirin 10%, aspirin 1%, mepyramine 5% and vehicle were applied to the inflamed and corresponding non-inflamed areas 20 min before itch induction with intradermal histamine injection. Itch and pain were scored on a visual analog scale at regular intervals. Wheal and flare areas were measured. No difference in itch intensities was found after application of aspirin, mepyramine and vehicle, but more itch was induced in aspirin and mepyramine pretreated sites in inflamed skin compared to normal skin (p < 0.05). In normal skin, flare areas were smaller after pretreatment with aspirin 10% (p < 0.05) and mepyramine (p < 0.001), as were wheal areas after mepyramine (p < 0.01), compared to vehicle pretreatments. In inflamed skin, flare areas were smaller after pretreatment with aspirin 10% (p < 0.01) and mepyramine (p < 0.001), as were wheal areas after aspirin 10% (p < 0.01), aspirin 1% (p <0.05) and mepyramine (p < 0.001). We conclude that despite a significant skin penetration as measured by the influence on wheal and flare reactions, topically applied aspirin did not decrease histamine-induced itch in the model used.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:835299 CAPLUS

DOCUMENT NUMBER: 136:145110

TITLE: A randomized parallel trial of topical aspirin-moisturizer solution vs. oral

aspirin for acute herpetic neuralgia

AUTHOR(S): Balakrishnan, Sadasivam; Bhushan, Kumar; Bhargava,

Vinod Kumar; Pandhi, Promila

CORPORATE SOURCE: Departments of Pharmacology and Dermatology,

Venereology, Postgraduate Institute of Medical Education and Research, Chandigarh, 160 012, India

SOURCE: International Journal of Dermatology (2001),

40(8), 535-538

CODEN: IJDEBB; ISSN: 0011-9059

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

Background In this study, the efficacy of oral aspirin vs. topical aspirin in moisturizer (Vaseline Intensive Care Lotion) was studied in an open, randomized, parallel trial in patients with acute herpetic neuralgia. Methods Thirty patients were evaluated in the trial, with 15 in each group. The patients were randomized to receive either oral aspirin, 375-750 mg three times a day, or 75 mg topical aspirin/mL of moisturizer (5-10 mL, depending on the extent of involvement), three times a day, for 21 days. Pain was assessed daily by means of a self-rating visual analog scale and physician assessment. In addition, the skin and plasma levels of aspirin were measured in both groups. Results The mean time to onset of pain relief was 44 min with topical aspirin and 110 min with oral aspirin. The mean duration of pain relief after a single application of topical aspirin was $5.4\ h$, whereas it was $3.5\ h$ with oral aspirin. The mean visual analog scale scores for pain with oral aspirin decreased from $68.2\,\pm\,6.1$ on day zero to 43.1 ± 8.7 on day 21, which was not significant compared with the baseline score. With topical aspirin, the baseline pain score was $77.5\,\pm\,3.7$ and decreased to $6.8\,\pm\,$ 3 on day 21 (P < 0.001 compared to the baseline score and compared to oral aspirin). The mean plasma and skin levels of aspirin

following oral administration were 16.21 \pm 1.1 μ g/mL and 1.97 \pm 0.3 $\mu g/mm2$, resp. After topical administration, the mean plasma level of aspirin was 2.29 \pm 0.5 $\mu g/mL$ (P < 0.01 vs. oral aspirin) and the skin level was 5.96 \pm 0.4 μ g/mm² (P

< 0.05 vs. oral aspirin). Treatment

tolerance was excellent in both groups. Conclusions This trial has demonstrated that topical aspirin in moisturizer is

clearly superior to oral aspirin in relieving the pain

of acute herpetic neuralgia, and that the analgesic activity of

aspirin is largely due to its local effect.

13 REFERENCE COUNT: THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:167792 CAPLUS

DOCUMENT NUMBER: 134:227363

Topical use of kappa opioid agonists to TITLE:

treat otic pain

Gamache, Daniel A.; Yanni, John M. INVENTOR(S):

Alcon Laboratories, Inc., USA PCT Int. Appl., 24 pp. PATENT ASSIGNEE(S):

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. ----

 WO 2001015678
 A2
 20010308

 WO 2001015678
 A3
 20020103

 WO 2000-US22766 20000818 <--

W: AU, BR, CA, CN, JP, MX, PL, TR, ZA

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-387359 A 19990831

Topical or intranasal compns. and methods for treating otic pain caused by otitis, surgery, or swimmer's ear are disclosed. In particular, the invention discloses compns. and methods of using κ -opioid agonists locally for the prevention or alleviation of otic pain. Compns. also comprise antimicrobial, antiallergy, and anti-inflammatory agents to treat otic infections, allergies, and inflammations associated with otic pain. For example, an otic/nasal solution contained (by weight) a κ -opioid EMD-61753 0.01-1.0%, phosphate buffered saline 1.0%, Polysorbate 80 0.5%, and water up to 100%.

ANSWER 7 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:167791 CAPLUS

134:227362 DOCUMENT NUMBER:

Use of 5-HT1B/1D agonists to treat otic pain TITLE:

INVENTOR(S): Gamache, Daniel A.; Yanni, John M.; Sharif, Najam A.
PATENT ASSIGNEE(S): Alcon Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 22 pp. INVENTOR(S):

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Englis LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE PATENT NO. ____

WO 2001015677 WO 2001015677 A2 20010308 WO 2000-US22764 20000818 <--

A3 20020328

W: AU, BR, CA, CN, JP, MX, PL, TR, US, ZA

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

PRIORITY APPLN. INFO.: US 1999-387358 A 19990831

Topical otic or intranasal compns. and methods for treating otic pain caused by otitis, surgery, or swimmer's ear are disclosed. In particular, the invention discloses compns. and methods of using 5-HT1B/1D agonists for the prevention or alleviation of otic pain . Compns. also comprise an antimicrobial, antiallergy, and anti-inflammatory agent to treat otic infections, allergies, and inflammations associated with otic pain. For example, an otic/nasal solution contained CGS-12066A 0.01-1.0%, phosphate buffered saline 1.0%, Polysorbate 80 0.5%, and water up to 100% (weight/volume), resp.

ANSWER 8 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:327685 CAPLUS

DOCUMENT NUMBER: 129:156440

ORIGINAL REFERENCE NO.: 129:31709a,31712a

TITLE: Skin and plasma levels of acetylsalicylic

> acid: a comparison between topical aspirin/diethyl ether mixture and oral aspirin in acute herpes zoster and

postherpetic neuralgia

Bareggi, S. R.; Pirola, R.; De Benedittis, G. AUTHOR(S):

CORPORATE SOURCE: Department of Pharmacology, University of Milan,

Milan, 20129, Italy

European Journal of Clinical Pharmacology (SOURCE:

1998), 54(3), 231-235

CODEN: EJCPAS; ISSN: 0031-6970

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal LANGUAGE: English

AB Objective: The aim of this investigation was to elucidate whether the analgesic effect was due to the local aspirin or to the systemic drug. This was done by comparing skin and plasma levels of acetylsalicylic acid (ASA) and salicylic acid (SA) after topically administered ASA/diethyl ether (ADE) mixture in acute herpetic neuralgia (AHN) and postherpetic neuralgia (PHN). The analgesia and the plasma and skin levels of ASA were also determined after oral administration of aspirin. Methods: Nineteen patients, 11 (57.9%) with AHN and 8 (42.1%) with PHN were given, on different days, a single 500-mg oral dose of ASA or a topical dose (750 mg) of (ADE) daubed onto the painful skin. The analgesic effect was assessed by a visual analog scale (VAS). Overall pain relief was graded as: excellent, good, fair, or poor. AHN as well as PHN patients had severe pain at baseline (6.83 and 5.93). Levels of ASA and SA in plasma and in the stratum corneum after adhesive tape stripping of the treated area were determined by HPLC. Results: After ADE application, the analgesic effect was very rapid and VAS scores were lower than at baseline. Pain significantly decreased by 82.6% after topical and 15.4% after oral ASA. After ADE, 95% of the patients had excellent or good pain relief, but after oral administration 79% of the patients had a poor response. Pain relief was similar in the two subgroups after ADE. Skin concns. of ASA, but not of SA, after ADE were about 80- to 100-fold those after oral administration. Levels of ASA and SA in plasma after oral administration were similar to those previously found, but after ADE were undetectable or very low. Patients with excellent pain relief showed a trend towards higher ASA

skin concns. Conclusions: The analgesic effect can be obtained only after topical administration, because by this route the skin levels of ASA are much higher than after oral administration. The mechanism is exclusively local; there are no active drugs in plasma after

topical administration.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:489273 CAPLUS

DOCUMENT NUMBER: 125:132614

ORIGINAL REFERENCE NO.: 125:24573a,24576a

TITLE: Topical aspirin/diethyl ether

mixture versus indomethacin and diclofenac/diethyl
ether mixtures for acute herpetic neuralgia and
postherpetic neuralgia: a double-blind crossover

placebo-controlled study

AUTHOR(S): Benedittis, Giuseppe De; Lorenzetti, Ariberto

CORPORATE SOURCE: Institute Neurosurgery, University Milan, Milan, Italy

SOURCE: Pain (1996), 65(1), 45-51

CODEN: PAINDB; ISSN: 0304-3959

PUBLISHER: Elsevier DOCUMENT TYPE: Journal LANGUAGE: English

The efficacy of topical aspirin/diethyl ether (ADE) mixture in the treatment of acute herpetic neuralgia and postherpetic neuralgia, suggested in a previous open-label study (De Benedittis et al. 1992), has been evaluated in a double-blind crossover placebo-controlled study as compared with two other NSAID (indomethacin and diclofenac) drug/ether mixts. The study included 37 patients (15 with acute herpetic neuralgia (AHN) and 22 with postherpetic neuralgia (PHN)). Comparative treatment results showed that only aspirin (but not indomethacin and diclofenac) was significantly superior to placebo, as compared with baseline and duration of pain relief (P < 0.05and P < 0.01, resp.), in both AHN and PHN groups. Good-to-excellent results were achieved by 87% of AHN patients and by 82% of PHN patients treated with the ADE mixture, with no significant differences between the two groups. On the whole, patients with trigeminal involvement, less severe pain and with dysaesthetic quality of pain yielded best results.

L6 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:232762 CAPLUS

DOCUMENT NUMBER: 124:306865 ORIGINAL REFERENCE NO.: 124:56559a

TITLE: Dose-dependent competitive block by topical

acetylsalicylic and salicylic acid of low $\operatorname{pH-induced}$

cutaneous pain

AUTHOR(S): Steen, Kay H.; Reeh, Peter W.; Kreysel, Hans W. CORPORATE SOURCE: Universitaets-Hautklinik Poliklinik, Universitaet

Bonn, Bonn, D-53105, Germany Pain (1996), 64(1), 71-82

CODEN: PAINDB; ISSN: 0304-3959

PUBLISHER: Elsevier DOCUMENT TYPE: Journal LANGUAGE: English

SOURCE:

AB In a human acid pain model, which used continuous intradermal infusion of a phosphate-buffered solution (pH 5.2) to induce localized nonadapting pain, the flow was adjusted to result in constant pain ratings of about 20% or 50% on a visual analog scale.

Volunteers participated in 4 different placebo-controlled double-blind

cross-over studies to measure rapidly evolving cutaneous analgesia from topically applied new ointment formulations of acetylsalicylic acid (ASA) and salicylic acid (SA) as well as of com. ibuprofen and benzocaine creams. Similar, log-linear dose-response curves were found for both ASA and SA, significant in effect at ≥ 3 g/kg and reaching saturation level at 15 and 30 g/kg, resp., which, 20 min after application, caused a mean pain suppression of 95% by ASA and 80% by SA. Half-maximal effects were achieved at 3 g ASA/kg and 15 g SA/kg. The SA action was also clearly slower to develop. With an increased flow of the acidic buffer, producing lower effective tissue pH and more intense pain, the effect of ASA and SA decreased to 73% pain suppression. A competitive mechanism of both drug effects was suggested by the fact that, with 15 g ASA or SA/kg, pain reduction could be reversed by increasing the buffer flow by a factor of 1.75. Com. ibuprofen (50 g/kg) and benzocaine creams (100 g/kg) were comparably as effective as ASA and SA, but the local anesthetic caused a loss of all cutaneous sensations, while the touch threshold with the specific analgesics was the same as with the placebo ointment. Thus, topical applications of nonsteroidal anti-inflammatory drugs dissolved in different ointment formulations have proven dose-dependently effective and specific in suppressing exptl. acidotic pain by a local and competitive mechanism.

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